

Diagnostic Testing Procedure for Acute Hepatic Porphyria (AHP)

additional information
on testing



When to suspect AHP¹⁻⁴

Acute symptoms/signs may include unexplained severe diffuse abdominal pain^a

+ One or more of:

- Nausea and vomiting
- Hyponatremia
- Muscle weakness
- Seizures
- Dark reddish to brownish urine

For more possible symptoms, please see overleaf



Note that even in absence of abdominal pain, AHP can present with neurologic, psychiatric, and other symptoms

Biochemical testing for diagnosis³⁻⁵

Simultaneous spot urine tests:

- PBG
- ALA
- Creatinine (for normalization per g or per mM creatinine)



Interpretation (elevations relative to ULN):^{3,5}

- ✓ PBG/ALA >3-fold
- ? PBG <3-fold/ALA ≥3-fold^b
- ? PBG/ALA <3-fold

If PBG/ALA <3-fold, retest. If test levels are normal but clinical suspicion is high then retest or consider second-line testing^c

Key Points

- Accurate AHP diagnosis and prompt treatment is essential to reduce complication risk
- Collect urine samples during an acute attack or near after when PBG/ALA are highest

When to genetic test?⁴⁻⁷

Genetic testing:

- Confirmation of AHP subtype
- Consider if biochemical tests are dubious and AHP suspicion remains high^c



Genetic testing can detect ≥95% of known mutations. Consult your genetic testing lab for further information. **Elevation of urinary PBG and/or ALA during an attack is sufficient for diagnosis.**

^aSymptoms suggestive of AHP vary and may also include other symptoms. Most but not all acute episodes feature severe diffuse abdominal pain and approximately 90% of patients with symptomatic AHP are women¹²;

^bIn a rare AHP subtype, patients have normal PBG and elevated ALA. Rule out lead poisoning and tyrosinemia to confirm AHP diagnosis^{3,5};

^cAdditional biochemical second-line testing may follow initial diagnosis and may include fecal and plasma testing for subtyping⁵.

Abbreviations: ALA, δ-aminolevulinic acid; g, gram; mM, millimole; PBG, porphobilinogen; ULN (per specific reference lab produced per lab), upper limit of normal. Please see overleaf for references

Acute Hepatic Porphyrria (AHP) Random Urine Testing Reference Guide

Random (spot) urine tests for elevated levels of PBG and ALA can help inform an AHP diagnosis^a

This guide provides testing information and protocols from national laboratories in the US for ordering PBG and ALA tests

Links to the sites for these independent laboratories are provided as a reference. Alnylam Pharmaceuticals does not endorse and is not responsible for the content on sites that are not operated by Alnylam Pharmaceuticals.

This testing and protocol information is provided for educational purposes only and is not intended to replace the independent medical judgment of any healthcare professional

	Lab/Test Code/CPT Code	Test Name	Synonyms/Related Terms	Random Urine Sample Requirements and Storage/Transportation Instructions				Rejection Criteria/ Causes for Rejection	Specimen Container and Collection
									
	ARUP-PBG/0080260/84110	Porphobilinogen (PBG), Urine*	PBG; Quantitative Porphobilinogen; Acute Porphyrria Screening Test	✓		✓		Not frozen; Exposed to light	Please visit ARUP Laboratories' online test directory www.aruplab.com for current specimen collection, transportation, and stability guidelines
	ARUP-ALA/2011474/82135	Aminolevulinic Acid (ALA), Random Urine	ALA; 5-Aminolevulinic Acid; Delta Aminolevulinic Acid; Delta ALA		✓		✓	Not refrigerated; Patient consumed alcohol within 24 hours	

*Random or 24-hour collection
For additional educational resources, visit arupconsult.com/content/porphyrias

	LabCorp-PBG/003065/84110*	Porphobilinogen (PBG), Quantitative, Random Urine	PBG Random Urine, Quantitative	✓		✓		Not frozen immediately; Exposed to light; pH >6 if ordered with Δ-ALA	Transfer 3 mL specimen to plastic urine container with 0.5 mL of 30% glacial acetic acid (optional preservative, required if ordered with Δ-ALA) and amber plastic frozen transport tube and cap (LabCorp No. 78656)
	LabCorp-ALA/007364/82135*	Δ-Aminolevulinic Acid, Random Urine	ALA, Delta, Random Urine	✓		✓		Not frozen immediately; Exposed to light; pH >7	Transfer 3 mL specimen to urine container with 0.5 mL of 30% acetic acid and amber plastic frozen transport tube and cap (LabCorp No. 78656)

*Also associated with CPT code 82570
For the most up-to-date testing and protocol information from LabCorp, please visit labcorp.com/test-menu/search

	Mayo-PBG/PBGU/84110	Porphobilinogen, Quantitative, Random, Urine	Acute Intermittent Porphyrria (AIP); Hereditary Coproporphyrria (HCP); PBG (Porphobilinogen); Variegate Porphyrria (VP)	✓		✓	✓	Not frozen immediately; Exposed to light; pH not >5.0; Patient consumed alcohol within 24 hours; List of current medications not provided	Transfer 20 mL specimen to amber 60 mL urine container (T596)
	Mayo-ALA/ALAU/82135	Aminolevulinic Acid, Urine	Acute Intermittent Porphyrria (AIP); ALA Dehydratase Deficiency Porphyrria (ADP); Delta-Aminolevulinic Acid; Hereditary Coproporphyrria (HCP); Variegate Porphyrria (VP); 5-Aminolevulinic Acid	✓	✓	Preferred	✓	Not frozen or refrigerated; Patient consumed alcohol within 24 hours; Patient's age is not provided	Transfer 2 mL specimen to 10 mL urine tube (T068)

For the most up-to-date testing and protocol information from Mayo Clinic, please visit mayocliniclabs.com

	Quest-PBG/6329/84110	Porphobilinogen, Quantitative, Random Urine*	PBG		✓	✓		Not refrigerated during transport; Exposed to light	Transfer 2 mL specimen (no preservative) to transport tube
	Quest-ALA/6301/82135	Delta Aminolevulinic Acid, Random Urine [†]	Delta-ALA; Porphyrria; Aminolevulinic Acid; D-Aminolevulinic Acid; D-ALA; ALA		✓	✓		Not refrigerated during transport; Exposed to light; First morning void, late evening specimen (after 8:00 PM), or specimen after excessive fluid intake	Transfer 2 mL of random urine (no preservative)

^aRandom or random clean-catch sample, light protected with aluminum foil, sent with sodium bicarbonate, with or without preservative, and optimal pH 6.0 to 7.0; [†]Random sample without preservative or preserved with 1 mL 6N HCl or 1 mL concentrated glacial acetic acid, and light protected with aluminum foil.

For the most up-to-date testing and protocol information from Quest Diagnostics, please visit testdirectory.questdiagnostics.com

 Sample to be frozen  Sample to be temperature controlled  Sample not to be exposed to light  No alcohol consumption within 24 hours

^aTo ensure greater accuracy, experts recommend that urine tests require normalization to urinary creatinine concentration per gram, and that specimens be collected during acute episodes. In most cases, 24-hour urine collection is not required. Additional testing (genetic or biochemical) may be required to differentiate AHP type (AIP, HCP, VP, and, ADP)

For labs not on this guide, confirm testing information and protocols in the lab's test directory by searching each of the test names: Aminolevulinic acid (ALA), Porphobilinogen (PBG)

Genetic testing of blood/saliva samples with targeted genetic tests or whole-genome sequencing to identify pathogenic variants associated with AIP (HMBS), HCP (CPOX), VP (PPOX), and ADP (ALAD) is available from the following laboratories in the US (CPT codes 81479, 81405, and 81406): Blueprint Genetics, Labcorp/Invitae, Mayo Clinic Laboratories, Mount Sinai Genetic Testing Laboratory, and Prevention Genetics

Abbreviations: ADP, acute delta-aminolevulinic acid deficiency porphyrria; AHP, acute hepatic porphyrria; AIP, acute intermittent porphyrria; ALA, aminolevulinic acid; ALAD, δ-aminolevulinic acid dehydratase; CPOX, coproporphyrinogen oxidase; CPT, Current Procedural Terminology; HCP, hereditary coproporphyrria; HMBS, hydroxymethylbilane synthase; PBG, porphobilinogen; PPOX, protoporphyrinogen oxidase; VP, variegate porphyrria

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During an acute AHP attack, patients can potentially experience any of the following symptoms and signs:*, 1-5, 8,9

CNS manifestations

- Confusion
- Altered mental status
- Anxiety
- Depression
- Tiredness
- Hallucinations
- Seizures

ANS manifestations

- Severe pain in the abdomen
- Chest or back pain
- Hypertension
- Tachycardia
- Nausea and vomiting
- Constipation
- Hyponatremia

PNS manifestations

- Neuropathic pain
- Peripheral neuropathy
- Sensory loss
- Muscle weakness
- Paralysis
- Respiratory failure

Cutaneous manifestations

- Lesions on sun-exposed skin

Other

- Dark reddish to brownish urine

*Symptoms suggestive of AHP vary and may also include other symptoms
Patients may also experience chronic symptoms, such as pain, tiredness, anxiety, and nausea¹



For additional scientific information related to AHP,
visit the Alnylam US Medical Affairs website at
RNAiScience.com/therapeutic-areas/acute-hepatic-porphyrin-ahp

Abbreviations: AHP, acute hepatic porphyria; ANS, autonomic nervous system; CNS, central nervous system; PNS, peripheral nervous system
References: 1. Gouya L et al. *Hepatology*. 2020;71:1546–58; 2. Thapar M et al. *Clin Exp Gastroenterol*. 2024;17:1–8; 3. Moghe A et al. *Hepatology*. 2025;82:1603–18;
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